CLAIMS

WHAT IS CLAIMED IS:

1. An isolated polynucleotide encoding an apyrase and/or NDPase and comprising a nucleotide sequence having at least about 80% sequence identity to a human polynucleotide selected from the group consisting of:

(a) a polynucleotide having the nucleotide sequence of SEQ ID NO. 2; and

(b) a polynucleotide having the protein coding nucleotide sequence of the polynucleotide sequence of (a).

2. An isolated polynucleotide encoding an apyrase and comprising a nucleotide sequence having at least about 90% sequence identity to a polynucleotide selected from the group consisting of:

(a) a polynucleotide having the nucleotide sequence of SEQ ID NO. 2; and

(b) a polynucleotide having the protein coding nucleotide sequence of the polynucleotide sequence of (a).

3. An isolated polynucleotide encoding a polypeptide with apyrase and/or NDPase activity, comprising a polynucleotide selected from the group consisting of:

(a) polynucleotides that encode the mature protein coding amino acid sequence of SEQ ID NO. 3.

4. An isolated polynucleotide encoding a polypeptide with apyrase and/or NDPase activity that hybridizes under stringent conditions to the complement of a polynucleotide of SEQ ID NO. 2.

5. The polynucleotide of any one of claims 1 through 4 which is a DNA.

6. The DNA of claim 5 which is a wholly or partially chemically synthesized DNA molecule.

7. An anti-sense polynucleotide which specifically hybridizes with the complement of the polynucleotide of claim 4.

8. The polynucleotide of claim 1 which comprises the nucleotide sequence of SEQ ID NO. 2 or 24 or the mature protein coding portions thereof.

9. An isolated polynucleotide which comprises a complement of the polynucleotide of claim 1.

10. An expression vector comprising the DNA of claim 5.

11. A host cell comprising the DNA of claim 5.

12. A host cell genetically engineered to express the DNA of claim 5.

13. An isolated human polypeptide with apyrase and/or NDPase activity comprising:

(a) the mature protein coding sequence of SEQ ID NO. 3; or

(b) an amino acid sequence having at least about 80% sequence identity to SEQ ID NO. 3.

14. An isolated polypeptide with apyrase and/or NDPase activity comprising:

(a) the CD39-like protein coding sequence of SEQ ID NO. 3; or

(b) an amino acid sequence having at least about 90% sequence identity to SEQ ID NO. 3.

15. The polypeptide of claim 13 or 14 which comprises the amino acid sequence of SEQ ID NO. 3 or 25 or the mature protein portions thereof.

16. The polypeptide of claim 13 or 14 wherein the polypeptide comprises at least one amino acid substitution selected from the group consisting of: D168→T, S170→Q and L175→F.

17. The polypeptide of claim 16 comprising a polypeptide having the amino acid sequence set forth in SEQ ID NO. 7.

18. A method for producing a CD39-like polypeptide comprising the steps of:

(a) growing a culture of cells according to claim 11 under conditions permitting expression of a CD39-like polypeptide; and

(b) isolating the CD39-like polypeptide from the host cell or its growth medium.

19. A composition comprising the polypeptide of claim 13, 14 or 15 and a pharmaceutically acceptable carrier.

20. An antibody specifically immunoreactive with a polypeptide encoded by the polynucleotide according to claim 1.

21. The antibody according to claim 20 which is a monoclonal antibody.

22. A hybridoma which secretes the antibody according to claim 21.

23. An anti-idiotype antibody specifically immunoreactive with the antibody according to claim 21.

24. A method for detecting a polynucleotide of claim 1, 2 or 3 in a sample comprising the steps of:

(a) contacting the sample with a compound that binds to and forms a complex with the polynucleotide for a period sufficient to detect the complex; and

(b) detecting the complex so that if a complex is detected, a polynucleotide of claim 1, 2 or 3 is detected.

25. A method for detecting a polynucleotide of claim 1, 2 or 3 in a sample comprising the steps of:

(a) contacting the sample under stringent hybridization conditions with nucleic acid primers that anneal to a polynucleotide of claim 1, 2 or 3 under such conditions; and

(b) amplifying the polynucleotides of claim 1, 2 or 3 so that if a polynucleotide is amplified, a polynucleotide of claim 1, 2 or 3 is detected.

26. The method of claim 25 wherein the polynucleotide is an RNA molecule that encodes a polypeptide of claim 13 or 14, and the method further comprises reverse transcribing an annealed RNA molecule into a cDNA polynucleotide.

27. A method for detecting a polypeptide of claim 13 or 14 in a sample comprising:

(a) contacting the sample with a compound that binds to and forms a complex with the polypeptide for a period sufficient to detect the complex; and

(b) detecting the complex so that if a complex is detected, a polypeptide of claim 13 or 14 is detected.

28. A method for identifying a compound that binds to a polypeptide of claim 13 or 14 comprising:

(a) contacting a compound with a polypeptide of claim 13 or 14 for a time sufficient to form a polypeptide/compound complex; and

(b) detecting the complex so that if a polypeptide/compound complex is detected, a compound that binds to a polypeptide of claim 13 or 14 is detected.

29. A method for identifying a compound that binds to a polypeptide of claim 13 or 14 comprising:

(a) contacting a compound with a polypeptide of claim 13 or 14, in a cell, for a time sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a reporter gene sequence in the cell, and

(b) detecting the complex by detecting reporter gene sequence expression so that if a polypeptide/compound complex is detected, a compound that binds to a polypeptide of claim 13 or 14 is identified.

30. A method of identifying a modulator compound of a CD39-like polypeptide with apyrase activity comprising the steps of:

(a) contacting the CD39-like polypeptide encoded by the polynucleotide of claim 1, 2 or 3 with a substrate in the presence and absence of a test compound;

(b) comparing apyrase activity of the CD39-like polypeptide in the presence and absence of the test compound; and

(c) identifying the test compound as a modulator compound when biological activity of the CD39-like polypeptide is increased or decreased in the presence of the test compound.

31. A method of identifying a modulator compound of a CD39-like polypeptide with NDPase activity comprising the steps of:

(a) contacting the CD39-like polypeptide encoded by the polynucleotide of claim 1, 2 or 3 with a substrate in the presence and absence of a test compound;

(b) comparing NDPase activity of the CD39-like polypeptide in the presence and absence of the test compound; and

(c) identifying the test compound as a modulator compound when biological activity of the CD39-like polypeptide is increased or decreased in the presence of the test compound.

32. A chimeric polypeptide comprising one or more domains of a CD39-like polypeptide fused to one or more domains of heterologous peptide or polypeptide, e.g., an immunoglobulin constant region.

33. A method of treatment comprising administering to a mammalian subject in need thereof a therapeutic amount of a composition comprising a polypeptide of claim 13 or 14 and a pharmaceutically acceptable carrier.

34. A method of treatment comprising administering to a mammalian subject in need thereof a therapeutic amount of a composition comprising an antibody that specifically binds to a polypeptide of claim 13 or 14 and a pharmaceutically acceptable carrier.

35. A method of inhibiting platelet function comprising administering the polypeptide of claim 13 or 14 to a medium comprising platelets.

36. A method of treating thrombotic diseases comprising administering a therapeutic amount of the polypeptide of claim 13 or 14 to a mammalian subject in need thereof.

37. A method of hydrolyzing nucleotidediphosphates comprising administering the polypeptide of claim 13 or 14 to a medium comprising nucleotidediphospates.

38. A method of inhibiting platelet aggregation in a mammalian subject comprising the step of reducing the ratio of ADP:ATP in said mammalian subject to a less than normal ratio.

39. The method of claim 38 wherein said ratio is reduced by administration of CD39-L4 having the sequence set forth in SEQ ID NO: 3 or a polypeptide having NDPase activity and at least about 90% sequence identity to SEQ ID NO: 3.

40. The method of claim 38 wherein said ratio is reduced by administration of CD39-L66 having the sequence set forth in SEQ ID NO: 25 or a polypeptide having NDPase activity and at least about 90% sequence identity to SEQ ID NO: 25.

41. The method of claim 38 wherein said ratio is reduced by administration of CD39-L2 having the sequence set forth in SEQ ID NO: 27 or a polypeptide having NDPase activity and at least about 90% sequence identity to SEQ ID NO: 27.

42. The method of claim 38 - 41 wherein the ratio of ADP:ATP is reduced systemically in circulation.

43. The method of claim 38 - 41 wherein the ratio of ADP:ATP is reduced locally within an area selected from the group consisting of heart, brain, kidney, lung and limbs.

44. The method of claim 38-41 wherein the ratio of ADP:ATP is reduced without significantly affecting ATP levels.

45. A method of identifying a compound capable of reducing the ratio of ADP:ATP to a less than normal ratio comprising the steps of:

(a) determining apyrase activity of said compound on ATP;

(b) determining apyrase activity of said compounds on ADP; and

(c) selecting a compound that has greater activity with respect to ADP compared to ATP.